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NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	SEP 09	CA/CAplus records now contain indexing from 1907 to the present
NEWS	4	AUG 05	New pricing for EUROPATFULL and PCTFULL effective August 1, 2003
NEWS	5	AUG 13	Field Availability (/FA) field enhanced in BEILSTEIN
NEWS	6	AUG 18	Data available for download as a PDF in RDISCLOSURE
NEWS	7	AUG 18	Simultaneous left and right truncation added to PASCAL
NEWS	8	AUG 18	FROSTI and KOSMET enhanced with Simultaneous Left and Righ Truncation
NEWS	9	AUG 18	Simultaneous left and right truncation added to ANABSTR
NEWS	10	SEP 22	DIPPR file reloaded
NEWS	11	SEP 25	INPADOC: Legal Status data to be reloaded
NEWS	12	SEP 29	DISSABS now available on STN
NEWS	13	OCT 10	PCTFULL: Two new display fields added

NEWS EXPRESS	OCTOBER 01 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 23 SEPTEMBER 2003
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FILE COVERS 1907 - 14 Oct 2003 VOL 139 ISS 16
FILE LAST UPDATED: 13 Oct 2003 (20031013/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> s microsphere and biodegradable and insulin
         11605 MICROSPHERE
         18947 MICROSPHERES
         21160 MICROSPHERE
                 (MICROSPHERE OR MICROSPHERES)
         23930 BIODEGRADABLE
            19 BIODEGRADABLES
         23942 BIODEGRADABLE
                 (BIODEGRADABLE OR BIODEGRADABLES)
        155313 INSULIN
          5150 INSULINS
        155389 INSULIN
                 (INSULIN OR INSULINS)
L1          59 MICROSPHERE AND BIODEGRADABLE AND INSULIN

=> s L1 and polylactic
          3314 POLYLACTIC
L2           5 L1 AND POLYLACTIC

=> d L2 1-5 ibib abs hitrn

L2   ANSWER 1 OF 5  CAPLUS  COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER:         2001:762783  CAPLUS
DOCUMENT NUMBER:          135:322723
TITLE:                    Proteins deposited onto sparingly soluble
                          biocompatible particles for controlled protein release
                          into a biological environment from a polymer matrix
INVENTOR(S):              Shih, Chung; Zentner, Gaylen; Piao, Ai-Zhi
PATENT ASSIGNEE(S):       Macromed, Inc., USA
SOURCE:                   PCT Int. Appl., 27 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     WO 2001076558      A1   20011018      WO 2001-US11217  20010406
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2002015737	A1	20020207	US 2001-827100	20010405
EP 1267838	A1	20030102	EP 2001-924765	20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001010319	A	20030729	BR 2001-10319	20010406
NZ 521994	A	20030829	NZ 2001-521994	20010406

PRIORITY APPLN. INFO.:

US 2000-195700P	P	20000407
US 2001-827100	A	20010405
WO 2001-US11217	W	20010406

AB The present invention relates to compns. and methods for the modulated release of one or more proteins or peptides. The compn. is comprised of a biocompatible polymeric matrix, a protein and/or peptide, and a sparingly water-sol. or essentially insol. particle. The protein is deposited by adsorption or some other mechanism onto the sparingly water-sol. biocompatible particle wherein the protein-particle combination is dispersed within the polymeric matrix. The deposition of the protein onto the particle acts to modulate the release of the protein or peptide from dosage forms including long-acting dosage systems. To a soln. of 5 mg/3mL human growth hormone was added to 100 mg of zinc carbonate and the suspension was allowed to stand in a refrigerator at 4.degree. for 16 h. HPLC anal. showed that the mass balance recovery of hGH, after removal of zinc using EDTA, was quant. In vivo pharmacokinetics of hGH sustained-release formulation was studied in rats.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 2001:300548 CAPLUS
DOCUMENT NUMBER: 134:316141
TITLE: Injection vehicle for polymer-based formulations
INVENTOR(S): Cleland, Jeffrey L.; Lam, Xanthe M.; Okumu, Franklin
PATENT ASSIGNEE(S): Genetech, Inc., USA
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001028591	A2	20010426	WO 2000-US26258	20001016
WO 2001028591	A3	20020307		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1220690	A2	20020710	EP 2000-971986	20001016
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.:

US 1999-159739P	P	19991015
WO 2000-US26258	W	20001016

AB The invention provides injection vehicles suitable for administering particulate suspensions, such as polymer-based formulations, as well as assocd. pharmaceutical formulations, articles of manuf., and kits. Other aspects of the invention included methods for producing and administering

pharmaceutical formulations. The injection vehicles of the invention are superior to conventional injection vehicles in that they include a pseudoplastic compn. that improves injectability, which facilitates delivery of the desired dose. The injection vehicles of the invention also allow the use of smaller-bore needles than are usually necessary to inject polymer-based formulations, reducing the pain assocd. with injection of such formulations. Syringeability of **microspheres** contg. proteins such as anti-rhGH Fab polymer-based formulations or VEGF, or other proteins and contg. Na hyaluronate was studied.

L2 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:513547 CAPLUS
DOCUMENT NUMBER: 133:125280
TITLE: Compositions and methods for controlled delivery of virus vectors
INVENTOR(S): Levy, Robert J.; Jones, Peter L.
PATENT ASSIGNEE(S): Children's Hospital of Philadelphia, USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043044	A1	20000727	WO 2000-US1193	20000119

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-116405P P 19990119
AB The invention relates to compns. and methods for delivering a virus vector to an animal. The compns. include compns. which comprise a matrix having a virus vector bound at the exterior surface thereof in a physiol. reversible manner. The invention also includes methods of making such compns., including particles, devices, bulk materials, and other objects which comprise, consist of, or are coated with such compns. Methods of delivering a virus vector to an animal tissue are also described.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1999:282075 CAPLUS
DOCUMENT NUMBER: 130:316644
TITLE: Encapsulation method using **biodegradable** polymers
INVENTOR(S): Laakso, Timo; Reslow, Mats
PATENT ASSIGNEE(S): Bioglan Therapeutics AB, Swed.
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9920253	A1	19990429	WO 1998-SE1717	19980924

W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

SE 9703874	A	19990424	SE 1997-3874	19971023
SE 512663	C2	20000417		
CA 2306824	AA	19990429	CA 1998-2306824	19980924
AU 9894670	A1	19990510	AU 1998-94670	19980924
AU 732891	B2	20010503		
EP 1033973	A1	20000913	EP 1998-948005	19980924
EP 1033973	B1	20030917		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001520186	T2	20011030	JP 2000-516653	19980924
ZA 9809199	A	19990415	ZA 1998-9199	19981008
NO 2000002039	A	20000613	NO 2000-2039	20000418

PRIORITY APPLN. INFO.: SE 1997-3874 A 19971023
WO 1998-SE1717 W 19980924

AB This invention provides a novel method of encapsulating an active substance in a **biodegradable** polymer, which comprises: (a) dissolving the **biodegradable** polymer in an org. solvent; (b) dispersing the active substance in the org. soln. obtained in step (a) to provide a dispersion with the active substance as the inner phase thereof, or alternatively, emulsifying the active substance, dissolved in water or other aq. solvent, in the org. soln. obtained in step (a) to provide an emulsion with the active substance as the inner aq. phase; and (c) subjecting the dispersion or emulsion to an encapsulation operation with an aq. polyethylene glycol soln. as a continuous phase to provide micro- or nanoparticles having the active substance encapsulated therein. A soln. of glycolide-lactide copolymer was prepd. by dissolving the polymer in EtOAc, then bovine serum albumin dissolved in a phosphate buffer was added to the polymer soln. The obtained homogeneous dispersion was slowly injected into the soln. of polyethylene glycol with stirring. Deionized water was added to reduce the viscosity of the suspension for filtration using a Millipore membrane. The filtrate was washed with water and dried to obtain spherical microparticles.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:149502 CAPLUS
DOCUMENT NUMBER: 128:184709
TITLE: **Microspheres** comprising a polymer and a drug dispersed within it
INVENTOR(S): Mathiowitz, Edith; Mullon, Claudy J. P.; Domb, Abraham J.; Langer, Robert S.
PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
SOURCE: U.S., 9 pp., Cont. of U. S. Ser. No. 304,702, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5718921	A	19980217	US 1996-691874	19960802

PRIORITY APPLN. INFO.: US 1987-25409 19870313
US 1989-304702 19890201

AB A method for prepn. of **biodegradable** polymeric drug delivery devices using relatively low temps. and non-aq. solns. which is particularly useful with polyanhydrides, thermolabile drugs, and in forming multi-layered devices. In a first embodiment, the polymer is dissolved in a volatile org. solvent, the drug is dispersed or dissolved in the polymer soln., the mixt. is suspended in an org. oil, and the org. solvent is extd. into the oil, creating **microspheres**. The preferred polymers are polyanhydrides since they are **biodegradable** and have been proven to be useful in vivo. In a second embodiment, the polymer is dissolved in org. solvent with or without the drug, and the mixt. is suspended in glycerol. The suspension is frozen and the org. solvent slowly evapd. Using these embodiments, alone or in combination with other methods including the "hot melt" technique, multi-walled **microspheres** having each wall degrading at a different rate or contg. different drugs can be manufd. **Microspheres** were prepd. from p-carboxyphenoxy propane-sebasic acid copolymer, silicone oil, and **insulin** according to above method. In vitro and in vivo release of **insulin** was studied.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s L1 and bicarbonate
43282 BICARBONATE
6388 BICARBONATES
47760 BICARBONATE
(BICARBONATE OR BICARBONATES)
L3 3 L1 AND BICARBONATE

=> d L3 1-3 ibib abs hitrn

L3 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2001:780648 CAPLUS
DOCUMENT NUMBER: 135:335147
TITLE: Polymer-based injectable sustained release pharmaceutical compositions for peptide and protein drugs
INVENTOR(S): Lee, Hee-yong; Lee, Hye-suk; Kim, Jung-soo; Kim, Sang-beom; Lee, Ji-suk; Choi, Ho-il; Chang, Seung-gu
PATENT ASSIGNEE(S): Peptron Inc., S. Korea
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078687	A1	20011025	WO 2001-KR462	20010322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1187602	A1	20020320	EP 2001-917893	20010322
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2003026844	A1	20030206	US 2002-18870	20020418
PRIORITY APPLN. INFO.:			KR 2000-20484 A	20000418

KR 2000-49344 A 20000824
WO 2001-KR462 W 20010322

AB Controlled and sustained release injectable pharmaceutical compns. for a biopharmaceutical, such as peptides and proteins are described. Processes for prepn. of an injectable sustained release compn. comprises (i) a step of prepg. **biodegradable** porous **microspheres** having accessible ionic functional groups, (ii) a step of encapsulating a biopharmaceutical into the **microspheres** through ionic interaction by suspending or equilibrating the **microspheres** in a soln. contg. the biopharmaceutical, and (iii) a step of recovering and freeze-drying the biopharmaceutical-incorporated **microspheres**. For example, **microspheres** were prepd. by water/oil/water double emulsion solvent evapn. method using a hydrophilic 50:50 PLGA polymer (RG 502H), which contains free carboxy end groups. Deionized water (800 mL) was added to 1 g of PLGA polymer dissolved in 2 mL of methylene chloride and emulsified by sonication for 30 s using a probe type ultrasonic generator. This primary emulsion was dispersed into 200 mL of deionized water contg. 0.5% polyvinyl alc. (wt./vol.) in a vessel which connected to a const. temp. controller and mixed well by stirring for 15 min at 2500 rpm, 25.degree. using a mixer. After mixing for another 15 min at 1500 rpm, 25.degree., temp. of continuous phase was increased to 40.degree. to evap. methylene chloride. After 1 h stirring at 40.degree., 1500 rpm, temp. was decreased to 25.degree.. The hardened **microspheres** were collected by centrifugation and washed twice with 200 mL of deionized water, and then freeze-dried. The **microspheres** obtained were used for incorporation of protein drugs, i.e., ovalbumin, bovine serum albumin, human growth hormone, RNase A, or lysozyme through ionic interaction by simply soaking and equilibrating the **microspheres** into a buffer soln. having an appropriate concn. of protein.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2000:880988 CAPLUS
DOCUMENT NUMBER: 134:46791
TITLE: Modified **biodegradable** polyester **microspheres** for stabilizing and improving the release profile of encapsulated drugs
INVENTOR(S): Bailey, Leonard C.; Shao, Pushpa G.
PATENT ASSIGNEE(S): Rutgers, the State University, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000074709	A2	20001214	WO 2000-US14875	20000530

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-137289P P 19990603

AB Modified **biodegradable microspheres** for encapsulation of a peptide or protein drug, e.g. **insulin**, made up of a **biodegradable** polymer and a basic excipient are provided. The **biodegradable** polymer comprises poly(L-lactic acid) or a copolymer

of L-lactic acid with D-lactic acid or glycolic acid, and the basic excipient comprises a **bicarbonate**. Also provided are methods of improving the release profile of a drug and delivering a drug to a patient via encapsulation of the drug within these modified **biodegradable microspheres**. For example, porcine **insulin microspheres** with a theor. **insulin** loading of approx. 3.2% contg. NaHCO3 (theor. loading level of 7.7%) were prepd. using Resomer RG 504 by an emulsion solvent evapn. method.

L3 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1999:742436 CAPLUS
DOCUMENT NUMBER: 132:83486
TITLE: Stabilization of pH-induced degradation of porcine **insulin** in **biodegradable** polyester **microspheres**
AUTHOR(S): Shao, Pushpa G.; Bailey, Leonard C.
CORPORATE SOURCE: Warner-Lambert Research Division, Morris Plains, NJ, USA
SOURCE: Pharmaceutical Development and Technology (1999), 4(4), 633-642
CODEN: PDTEFS; ISSN: 1083-7450
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose of this research project was to stabilize the pH-induced degrdn. of porcine **insulin** encapsulated within **biodegradable** polyester **microspheres** through the incorporation of a basic additive. **Insulin microspheres** fabricated using Poly(L-lactide) (L-PLA) and Poly(DL-lactide-co-glycolide) (50:50 DL-PLGA) were subjected to in vitro release studies and the stability of unreleased **insulin** encapsulated within **microspheres** was investigated. The intramicrosphere pH was estd. by encapsulating acid-base indicators covering a wide pH transition range within 50:50 DL-PLGA **microspheres**. Finally, a basic excipient sodium **bicarbonate** was incorporated in 50:50 DL-PLGA **microspheres** to minimize acid-induced **insulin** degrdn. The in vitro release was slow and incomplete (<30% in 30 days). Extn. and analyses of the unreleased **insulin** within the **microspheres** revealed that an av. of .apprx.11% remained intact. The degrdn. products obsd. consisted of .apprx.15% of three distinct deamidated hydrolysis products including A-21 Desamido **insulin**, .apprx.22% Covalent **Insulin** Dimer and trace amts. of High Mol. Wt. Transformation Products. Comparison of the degrdn. profile of unreleased **insulin** contained in various **microsphere** formulations with the in vitro release kinetics indicated that an increase in covalent dimer formation within the **microspheres** prior to release is assocd. with a decrease in the cumulative percent **insulin** released during a 30-day incubation period. In an attempt to correlate **insulin** degrdn. with the drop in intra-**microsphere** pH due to polymer hydrolysis, it was detd. that the pH within a degrading **microsphere** reaches a value of .apprx.1.8 after 4 wk. The incorporation of a basic excipient, sodium **bicarbonate**, in 50:50 DL-PLGA **microspheres** resulted in an improved in vitro release profile (cumulative release .apprx.47.3% in 30 days) as well as a significant redn. in covalent dimerization of the unreleased **insulin** to barely detectable levels. The low pH microenvironment within a degrading **microsphere** is one of the major factors leading to protein instability, and the degrdn. of proteins encapsulated within polyester **microspheres** can be minimized by the incorporation of a basic excipient.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file stnguide

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	29.60	29.81

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.21	-5.21

FILE 'STNGUIDE' ENTERED AT 13:29:12 ON 14 OCT 2003

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 10, 2003 (20031010/UP).